the test group, subjects are administered a compound of the invention at a variety of times prior to, during and after exposure to HBV. The effects of the compound on the test group are compared to the effects observed in the control group, e.g., through physical observation and examination of the subjects and through blood or serum analysis to determine at what point in time the infection is cleared from the subject. For example, assays are run to detect the presence and/or amount of hepatitis B virus called surface antigens and fragments thereof. Alternatively or in addition, the subject's liver is analyzed. Liver function tests analyze levels of certain proteins and enzymes, such as, for example, aspartate aminotransferase (AST, formerly serum glutamic-oxaloacetic transaminase (SGOT)) and alanine aminotransferase (ALT, formerly serum glutamate-pyruvate transaminase (SGPT)).

Example 18: The Effect of Compounds on Tyrosine Kinase Inhibition

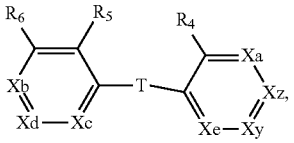
[0680] The following example illustrates that the compounds of the present invention could be used to treat autoimmune diseases. The compounds are tested using a method described previously (Goldberg, et al.; 2003, *J. Med. Chem.,* 46, 1337-1349). The kinase activity is measured using DELFIA (dissociation enhanced lanthanide fluoroimmunoassay), which utilizes europium chelate-labeled anti-phosphotyrosine antibodies to detect phosphate transfer to a random polymer, poly-Glu4-Tyrl (PGTYR). The kinase assay is performed in a neutravidin-coated 96-well white plate in kinase assay buffer (50 mM HEPES, pH 7.0, 25 mM MgCl2, 5 mM MnC12, 50 mM KCl, 100 μM Na3VO4, 0.2% BSA, 0.01% CHAPS). Test samples (compounds of the instant invention) initially dissolved in DMSO at 1 mg/mL are prediluted for dose response (10 doses with starting final concentration of 1 μg/mL, 1-3.5 serial dilutions) with the assay buffer. A 25 μL aliquot of this diluted sample and a 25 μL aliquot of diluted enzyme (lck) (0.8 nM final concentration) are sequentially added to each well. The reaction is started with a 50 μL/well of a mixture of substrates containing 2 μM ATP (final ATP concentration is 1 μM) and 7.2 ng/μL PGTYR-biotin in kinase buffer. Background wells are incubated with buffer and substrates only. Following 45 min of incubation at room temperature, the assay plate is washed three times with 300 μL/well DELFIA wash buffer. A 100 μL/well aliquot of europium-labeled anti-phosphotyrosine (Eu^{3+}-PT66, 1 nM, Wallac CR04-100) diluted in DELFIA assay buffer is added to each well and incubated for 30 min at room temperature. Upon completion of the incubation, the plate is washed four times with 300 μL/well of wash buffer and 100 μL/well of DELFIA wash buffer. Enhancement solution (Wallac) is added to each well. After 15 min, timeresolved fluorescence is measured on the LJL's analyst (excitation at 360 nm, emission at 620 nm, EU 400 dichroic mirror) after a delay time of 250 μs. The compound of the instant invention could inhibit the kinase activity of lck, indicating that the compound may be used to treat autoimmune disease in a subject.

Other Embodiments

[0681] While the invention has been described in conjunction with the detailed description thereof, the foregoing description is intended to illustrate and not limit the scope of the invention, which is defined by the scope of the appended claims. Other aspects, advantages, and modifications are within the scope of the following claims. It will be understood by those skilled in the art that various changes in form and details may be made therein without departing from the scope of the invention encompassed by the appended claims.

1. A compound according to Formula IA

(Formula IA)



or a salt, solvate, hydrate, or prodrug thereof, wherein: T is absent, $CR_{12}R_{13}$, C(O), O, S, S(O), $S(O)_2$, NR_{14}, $C(R_{15}R_{16})$ $C(R_{17}R_{18})$, CH_2O, or OCH_2;

X_y is CZ, CY, N, or N—O;

X_z is CZ, CY, N, or N—O;

at least one of X_y and X_z is CZ;

Y is selected from hydrogen, hydroxyl, halogen, lower (C_1, C_2, C_3, C_4, C_5, or C_6) alkyl, C_1, C_2, C_3, C_4, C_5, or C_6 alkoxy, O-lower (C_1, C_2, C_3, C_4, C_5, or C_6) alkyl-aryl, and O-benzyl;

X_a is CR_a or N, or N—O;

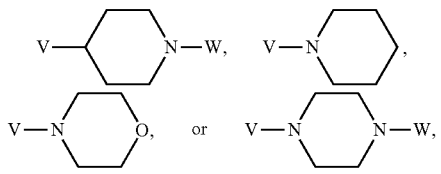
X_b is CR_b, N, or N—O;

X_c is CR_c or N, or N—O;

X_d is CR_d or N, or N—O;

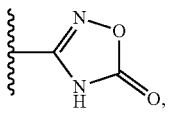
X_e is CR_e, N, or N—O;

R_a, R_b, R_c, R_d, R_e, R_4, R_5, and R_6 are, independently, hydrogen, hydroxyl, halogen, P, C_1, C_2, C_3, C_4, C_5, or C_6 alkyl, C_1, C_2, C_3, C_4, C_5, or C_6 alkoxy, O-lower (C_1, C_2, C_3, C_4, C_5, or C_6) alkyl-aryl, O-benzyl, C_1, C_2, C_3, C_4, C_5, or C_6 alkyl-OH, COOH, COO-lower (C_1, C_2, C_3, C_4, C_5, or C_6) alkyl, SO_2H, SO_2-lower (C_1, C_2, C_3, C_4, C_5, or C_6) alkyl,



wherein W is H, or C_1, C_2, C_3, C_4, C_5, or C_6 alkyl, C_1, C_2, C_3, C_4, C_5, or C_6 alkyl-aryl;

P is SO_3H, OSO_3H, OPO_3H_2, OPO_3H_2, NH_2, NHR_{19}, NHR_2OR_{21},



tetrazole, O-lower (C_1, C_2, C_3, C_4, C_5, or C_6) alkyl-K, O—C(O)-lower (C_1, C_2, C_3, C_4, C_5, or C_6) alkyl-L, NH-lower (C_1, C_2, C_3, C_4, C_5, or C_6) alkyl-M, or O-aryl-Q, further wherein lower (C_1, C_2, C_3, C_4, C_5, or C_6) alkyl is linear or branched alkyl;